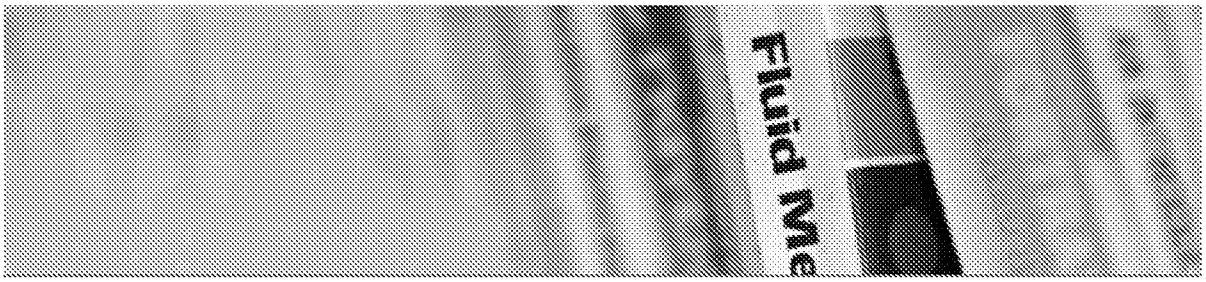

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Differentiation induction in non-lymphocytic leukemia cells upon treatment with mizoribine

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Résumé / Abstract
Copyright (c) 1997 Elsevier Science Ireland Ltd. All rights reserved. Inosine-5<precedes>-monophosphate (IMP) dehydrogenase catalyzes the rate-limiting reaction of guanine nucleotide biosynthesis and has been implicated in the reaction of cell growth and differentiation. We examined the ability of mizoribine, an IMP dehydrogenase inhibitor, to induce differentiation in HL-60 and U937 cells as well as in fresh leukemic blast cells from patients with non-lymphocytic leukemia. Treatment with mizoribine reduced intracellular GTP levels and induced morphologic and functional differentiation in these two cell lines in a dose-dependent manner. HL-60 and U937 cells developed polymorphic nuclei and macrophage-like cytoplasm, respectively, as well as expression of CD11b and CD14 antigens and the ability to oxidize NBT. These changes became evident when intracellular GTP levels decreased to approximately 30% of untreated controls and were abrogated by addition of guanosine to the media. However, in fresh leukemic cells, the cells showing maturation in response to mizoribine were limited in those derived from two of ten patients having non-lymphocytic leukemia. These findings suggest mizoribine could induce differentiation in HL-60 and U937 cells through a decrease of intracellular GTP levels. Further study is required to determine its clinical use in patients with acute non-lymphocytic leukemia. © 1997 Elsevier Science Ireland Ltd.

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